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ORIGINAL ARTICLE

Factors associated with glycemic control in type 1 diabetes patients in China: A cross-sectional study

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ABSTRACT

Aims/Introduction: Glycemic control in type 1 diabetes can be challenging, and is influenced by many factors. This study aimed to investigate glycemic control and its associated factors in Chinese people with type 1 diabetes.

Materials and Methods: This cross-sectional study included 779 participants with type 1 diabetes selected from hospital records review, outpatient clinics and inpatient wards. Data were collected through face-to-face interviews, medical records and venous blood samples. Multiple logistic regression analysis was carried out to determine factors associated with glycemic control.

Results: Among 779 participants, 49.2% were male. The median age was 24 years (interquartile range 14–36 years). The median age at diagnosis of diabetes was 17 years (interquartile range 10–28 years) and the median duration of diabetes was 4 years (interquartile range 1–8 years). The mean ± standard deviation hemoglobin A1c was 9.1 ± 2.5%. Nearly 80% of participants had inadequate glycemic control (hemoglobin A1c ≥7.0%). Multivariable analysis showed that age at diagnosis of diabetes ≤20 years, living in a rural location, low household income, low intake of fruit and vegetables, low level of physical activity, low adherence to insulin, and low utilization of insulin pump were independent risk factors for poor glycemic control (hemoglobin A1c ≥9.0%).

Conclusions: Inadequate glycaemic control is common among people with type 1 diabetes in China. Efforts should be made to control the modifiable risk factors, which include low intake of fruit and vegetables, low level of physical activity, and low adherence to insulin for the improvement of glycemic control. Appropriate use of insulin pump among type 1 diabetes should be encouraged.

INTRODUCTION

The Diabetes Control and Complications Trial and its follow-up Epidemiology of Diabetes Interventions and Complications study showed that improved glycemic control over a prolonged period leads to the reduction of the risk of microvascular and macrovascular complications among type 1 diabetes patients[1,2]. Recently, international and Chinese guidelines set a target hemoglobin A1c (HbA1c) of 6.5–7.5% for most people with type 1 diabetes. Despite the release of insulin analogs, and the development of sophisticated insulin delivery and glucose monitoring systems to improve diabetes care over the past few decades, glycemic control in type 1 diabetes is still inadequate in many studies. Data from the T1D Exchange clinic registry including 25,833 adults and children with type 1 diabetes in the USA showed that the overall average HbA1c was 8.3% at enrollment. Control was the worst among those aged 13–25 years[3]. A multinational study of 19 countries showed that the majority of people with type 1 diabetes failed to achieve the target of HbA1c recommended by guidelines, and there were wide variations in glycemic control across countries and data

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sources[4]. The proportions with HbA1c ≥7.5% were 66.2% in data from clinics and 73.0% in data from population-based data sources. Another study from China among adults with type 1 diabetes reported that only one-fifth of participants met the target of HbA1c <7%[5]. However, there are scarce data reporting glycemic control in type 1 diabetes covering all age groups in China.

Glycemic control in type 1 diabetes is often complex and affected by many factors. Thus, identifying barriers to optimal glycemic control might help to improve the outcomes and the quality of healthcare services. Several studies have assessed risk factors for glycemic control among type 1 diabetes. Sociodemographic factors, such as age, sex, family dynamics and social disadvantage, appear important in many studies[6-8]. Other factors, such as diabetes duration, parental involvement and adherence to treatment, have also been reported to be strongly correlated with glycemic control[9,10]. However, much of these data arise from high-income countries, and limited data exist in China. Among the scant Chinese data, one study found that clinic visit frequency, tobacco use, frequency of self-monitoring of blood glucose (SMBG), islet cell autoantibodies and fasting C-peptide levels were related to glycemic control[5]. However, that study only included adults with type 1 diabetes, and did not investigate dietary intake and physical activity as potential factors associated with glycemic control.

The objective of the present study was to evaluate the current status of glycemic control, and to identify its associated factors among Chinese patients with type 1 diabetes. This will help to develop targeted interventions to improve glycemic control and prevent diabetic complications in this population.

METHODS

Data source

This study was carried out as a part of The Type 1 Diabetes Mellitus in China 3C: Coverage, Costs and Care Study (3C study), which examines the coverage, cost and care of type 1 diabetes in two cities of China: Beijing and Shantou. The International Diabetes Federation in collaboration with the Chinese Diabetes Society designed the study, which included six primary, five secondary and six tertiary healthcare institutions that had active diabetes outpatient clinics. The design of the 3C study has been published in detail previously[6]. Participants were enrolled sequentially from a 3-year retrospective review of hospital records. In total, 849 participants were recruited sequentially from the record review, outpatient clinics and inpatient wards. Trained investigators carried out face-to-face interviews with participants or their parents (if aged <15 years) between July and September 2011, and January and February 2012. We excluded people aged <6 months at type 1 diabetes diagnosis. Waist circumference was measured at the point halfway between the inferior costal margin and the iliac crest in a horizontal plane. Blood pressure was measured twice with a sphygmomanometer after sitting for at least 10 min. The average of the readings was taken. Venous blood samples were collected and assayed at local hospital laboratories for lipids and HbA1c. We excluded 70 participants due to the missing HbA1c data in the present analysis, leaving 779 participants for analyses.

Written informed consent was provided by adult participants or parents/guardians if aged <15 years. The study was approved by the ethics committees of Beijing Children's Hospital, Peking University Health Science Center, the First Affiliated Hospital of Shantou University Medical College and the Second Affiliated Hospital of Shantou University Medical College.

Definition of type 1 diabetes

All participants had documented diagnosis of type 1 diabetes after 6 months-of-age. In addition, at least one of the following conditions was required: (i) age at diagnosis ≤35 years; (ii) fasting and stimulated C-peptide levels <0.2 nmol/L; (iii) episodes of repeated ketosis, ketoacidosis and/or uncontrolled hyperglycaemia during the first 6 months after diagnosis; (iv) episodes of repeated ketosis, ketoacidosis and/or uncontrolled hyperglycemia in the absence of insulin therapy for >1 week; and (v) signs of repeated ketosis, ketoacidosis and/or uncontrolled hyperglycemia if prescribed oral antihyperglycaemic agents, which were relieved with insulin administration[7].

Operational definitions of risk factors

Glycemic control was categorized into adequate control (HbA1c <7.0%), suboptimal control (7.0% ≤ HbA1c < 9.0%) and poor control (HbA1c ≥ 9.0%) groups. Elevated waist circumference for those aged ≤18 years was defined as ≥90th percentile, based on a study from the Chinese population with sex- and age-specific percentiles[8]. For adults, elevated waist circumference was defined as ≥80 cm for women and ≥90 cm for men[9]. Hypertension was defined as either a documented diagnosis of hypertension, antihypertensive treatment or three previous readings of high blood pressure (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg). Dyslipidemia was defined as low-density lipoprotein cholesterol ≥2.6 mmol/L (77.3 mg/dL). Diabetes diet was defined as a balanced diet that is recommended by nutritionists or endocrinologists based on personal preferences and physical activity. A controlled diet was defined as ≥5 days of meals per week following the instructions of the diabetes diet. Frequent intake of fruit and vegetables was defined as ≥5 days in a week following the recommendation on the intake of fruit and vegetables (≥5 servings of fruit and vegetable per day. A serving of fruit and vegetables is equal to 125 mL in volume). The total time of physical activity in a week was categorized into ≥150 min and <150 min. A non-smoker was defined as someone who had not smoked one or more cigarettes during the past year before enrollment. Insulin regimen was categorized as either as intensive or less intensive regimen. Intensive regimen was defined as receiving insulin injections three or more times per day or using an insulin pump. SMBG adherence was determined by the number of days of blood glucose tested in the previous week, and was graded as adequate (≥5 days) and inadequate adherence (<5 days). Insulin adherence was determined by the number of days of insulin doses missed in the past week, and was graded as high (≤2 days) and low adherence (>2 days).

Statistical analysis

All data analyses were carried out using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Data were presented as the median (25th, 75th quartile) and mean ± standard deviation for continuous variables, and as *n* (%) for categorical variables. Univariate associations between levels of glycemic control in categories and risk factors were examined using χ^2-tests. Risk factors with a *P*-value <0.2 from univariate analyses were entered into a multiple logistic regression with stepwise variable selection. A multiple logistic regression analysis with HbA1c categorized based on HbA1c level<9% and HbA1c ≥9% was used to determine the independent risk factors. Statistical significance was defined by a *P*-value <0.05.

RESULTS

Study characteristics

The approach used for participants' selection is shown in Figure 1. After exclusions, 779 participants with type 1 diabetes were included in the study, 49.2% of whom were males. A total of 464 participants (59.6%) were from Beijing, and 315 (40.4%) were from Shantou. The median age at diagnosis of diabetes was 17 years (interquartile range 10–28 years). The median duration of diabetes was 4 years (interquartile range 1–8 years). The mean ± standard deviation HbA1c was 9.1 ± 2.5%. Just 20.2% of participants had good glycemic control (HbA1c <7.0%), 36.7% had suboptimal glycemic control (9.0% > HbA1c ≥ 7.0%) and 43.1% had poor glycemic control (HbA1c ≥9.0%). A total of 89 participants (11.4%) were on an insulin pump.

Comparison of variables by levels of glycemic control

Demographic characteristics of the participants by different levels of glycemic control are shown in Table 1. There was a higher prevalence of poor glycemic control among males and those aged ≤40 years. A significantly higher proportion of those with lower household income, lower levels of education attainment and those living in a rural location had poor glycemic control. Insurance status was not significantly associated with glycemic control. Participants' clinical and lifestyle characteristics by levels of glycemic control are summarized in Table 2. The proportion of participants with poor control was higher among participants with age at diagnosis of diabetes <20 years, higher levels of low-density lipoprotein cholesterol, those who were taking fewer than three injections of insulin per day and among those who had low adherence to insulin. Duration of diabetes and hypertension did not appear to be associated with glycemic control. Higher proportions of those with uncontrolled diet and inadequate adherence to SMBG had poor glycemic control; however, the associations were not statistically significant. Glycemic control was also worse among those with less frequent intake of fruit and vegetables, and those with physical activity <150 min/week. Smoking status did not differ among different categories of glycemic control.

Factors independently associated with poor glycemic control

The results of the multiple logistic regression analysis are summarized in Figure 2. Glycemic control was found to be very poor (HbA1c ≥9.0%) in 336 participants (43.1%). Age at diagnosis <20 years increased the risk of poor control by 73%, as compared with age at diagnosis ≥20 years. Living in a rural location was associated with a 1.7-fold higher risk of poor control. Lower household income was associated with a 47% higher risk of poor control. Less frequent intake of fruit and vegetables was associated with a 48% higher risk of poor control, whereas a low level of physical activity was associated with a 91% higher risk of poor control. Low adherence to insulin increased the risk of poor control by 1.5-fold. Utilization of an insulin pump reduced the risk of poor glycemic control by 58%. Other factors, such as age, sex, highest education level of family members, insurance status, smoking status, waist circumference, diet control status, insulin regimen and adherence to self-monitoring of blood glucose, were not associated with glycemic control in the present study.

DISCUSSION

In the present cross-sectional study, we evaluated the status of glycemic control and its associated factors among Chinese with type 1 diabetes. We found that 20.2% of people with type 1 diabetes reached an HbA1c target <7%, showing a gap between guidelines and clinical practice. The proportion of people with type 1 diabetes achieving optimal glycemic control is comparable with that reported in another Chinese population with type 1 diabetes[5]. However, the mean HbA1c level (9.1%) in the present population was much higher than that (8.3%) from data of the T1D Exchange clinic registry in the USA[3]. Recently, a study using data from eight high-income countries for people with type 1 diabetes aged <18 years found that the mean HbA1c varied from 7.6% to 8.8%. Sweden reported the lowest mean HbA1c, followed by Germany and Austria[10]. This was lower than the mean HbA_{1c} level among those aged <20 years of 9.2% in the present study, highlighting the need to increase the understanding of the barriers of care in type 1 diabetes.

The present study has allowed a more detailed evaluation of the underlying factors that might contribute to poor glycemic control in type 1 diabetes. Factors associated with glycemic control included age at diagnosis of diabetes, location of residence, household income, daily intake of fruit and vegetables, physical activity, adherence to insulin, and utilization of an insulin pump. Some of these factors are not commonly reported as factors contributing to poor control in type 1 diabetes patients. For example, the role of the age at diagnosis of diabetes in the management of type 1 diabetes has rarely been described. However, several studies found that younger age and longer duration of diabetes were associated with poor glycemic

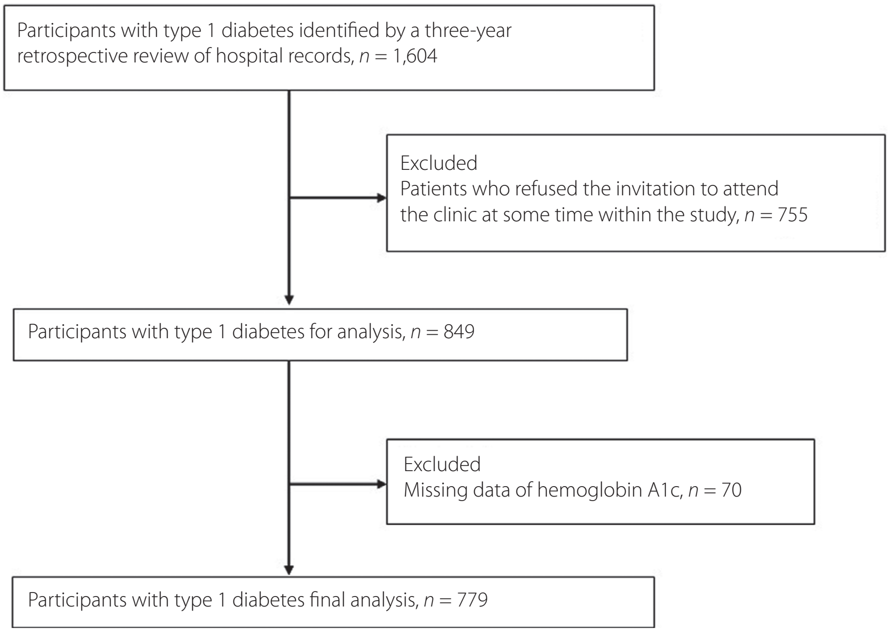

Figure 1 | Detailed approach for participant selection.

Table 1 | Demographic characteristics of people with type 1 diabetes by hemoglobin A1c levels

	HbA1c < 7.0% n = 157	7.0% ≤ HbA1c < 9.0% n = 286	HbA1c ≥ 9.0% n = 336	*P*-value
Sex, % (*n*)				
Males	16.4 (63)	37.3 (143)	46.2 (177)	0.032
Females	23.7 (94)	36.1 (143)	40.2 (159)	
Age, % (*n*)				
>40 years	20.1 (30)	48.3 (72)	31.5 (47)	0.009
20–40 years	21.9 (66)	32.9 (99)	45.2 (136)	
≤20 years	18.3 (60)	35.2 (115)	46.5 (152)	
Household income, % (*n*)				
≥¥4,000/month	23.8 (82)	43.6 (150)	32.6 (112)	0.000
<¥4,000/month	17.6 (70)	30.7 (122)	51.8 (206)	
Highest education level of family members, % (*n*)				
Less than Bachelor's degree	16.8 (87)	34.1 (177)	49.1 (255)	0.000
Bachelor's degree or more	27.1 (68)	42.6 (107)	30.3 (76)	
Location of residence, % (*n*)				
Rural area	16.0 (54)	27.8 (94)	56.2 (190)	0.000
Urban area	23.8 (101)	43.1 (183)	33.2 (141)	
Insurance status				
Without insurance	22.7 (20)	31.8 (28)	45.5 (40)	0.578
With insurance	19.8 (137)	37.3 (258)	42.8 (296)	

control[11,12]. Age at diagnosis was calculated as the current age minus duration of diabetes, and it is difficult to determine the separate effects of duration and age at diagnosis. The present study showed that age at diagnosis <20 years was associated with a 73% higher risk of poor control, as compared with age at diagnosis ≥20 years. A possible explanation for this finding is that patients with a younger age at diagnosis have a more rapid and extensive loss of β-cells, contributing to poor glycemic control. Studies examining the pancreas of patients with recent-onset type 1 diabetes showed that those diagnosed

Table 2 | Clinical and lifestyle characteristics of people with type 1 diabetes by hemoglobin A1c levels

	$HbA_1c < 7.0\%$ *n* = 157	$7.0\% \leq HbA1c < 9.0\%$ *n* = 286	$HbA1c \geq 9.0\%$ *n* = 336	*P*-value
Age at diagnosis, % (*n*)				
≥20 years	21.1 (75)	40.8 (145)	38.0 (135)	0.025
<20 years	19.1 (81)	33.3 (141)	47.5 (201)	
Duration of diabetes % (*n*)				
≥5 years	17.9 (60)	41.2 (138)	40.9 (137)	0.071
<5 years	21.9 (97)	33.4 (148)	44.7 (198)	
Waist circumference, % (*n*)				
Normal	18.2 (109)	38.1 (228)	43.6 (261)	0.048
High	25.9 (30)	27.6 (32)	46.4 (54)	
Dyslipidemia, % (*n*)				
No	22.5 (73)	38.9 (126)	38.6 (125)	0.002
Yes	16.6 (57)	31.5 (108)	51.9 (178)	
Hypertension, % (*n*)				
No	21.1 (128)	37.2 (226)	41.7 (253)	0.104
Yes	12.6 (14)	38.7 (43)	48.6 (54)	
Diet control status				
Controlled	21.5 (119)	38.0 (210)	40.5 (224)	0.060
Uncontrolled	16.8 (38)	33.6 (76)	49.6 (112)	
Fruit and vegetables, % (*n*)				
Frequent	20.8 (95)	41.4 (189)	37.7 (172)	0.001
Less frequent	19.2 (62)	30.0 (97)	50.8 (164)	
Physical activity, % (*n*)				
≥150 min/week	22.5 (106)	41.0 (193)	36.5 (172)	0.000
<150 min/week	16.6 (51)	30.2 (93)	53.2(164)	
Smoking status, % (*n*)				
Non-smoker	20.8 (138)	36.2 (241)	43.0 (286)	0.577
Smoker	16.7 (19)	39.5 (45)	43.9 (50)	
Insulin regimen, % (*n*)				
Intensive	19.9 (86)	43.0 (186)	37.2 (161)	0.000
Less intensive	20.4 (69)	29.2 (99)	50.4 (171)	
Adherence to self-monitoring blood glucose				
Adequate	24.2 (72)	36.4 (108)	39.4 (117)	0.062
Inadequate	17.6 (85)	36.9 (178)	45.4 (219)	
Adherence to insulin				
High	20.1 (142)	38.8 (275)	41.1 (291)	0.000
Low	21.1 (15)	15.5 (11)	63.4 (45)	

before the age of 7 years have a much lower proportion of residual insulin-containing islets (14 ± 3%) than those diagnosed beyond the age of 13 years (39 ± 4%)[13,14].

We also found that living in rural areas and lower household income significantly increased the risk of poor control, which is consistent with other previous studies. Secrest *et al.*[15] found that income level was inversely associated with HbA1c levels and the incidence of diabetes complications in the Pittsburgh EDC study. In 2015, another study from the UK used the Scottish Index of Multiple Deprivation, which is based on current income, residence, housing and health to evaluate socioeconomic status, and showed a linear association between socioeconomic status and glycemic control in type 1 diabetes[16]. As with many healthcare regimens, the financial burden on families to maintain good metabolic control is considerable. Lower household income and living in rural areas might be associated with poor self-management, possibly as a result of lack of access to medical care or unaffordability of good health care (i.e., insulin delivery devices and blood glucose testing strips). These findings highlight the need for strategies to ensure that type 1 diabetes patients with low socioeconomic status obtain adequate diabetes care and routine follow up to improve glycemic control and reduce their risk of complications.

Healthy diet and active physical activity are key components in the management of type 1 diabetes. In the present study,

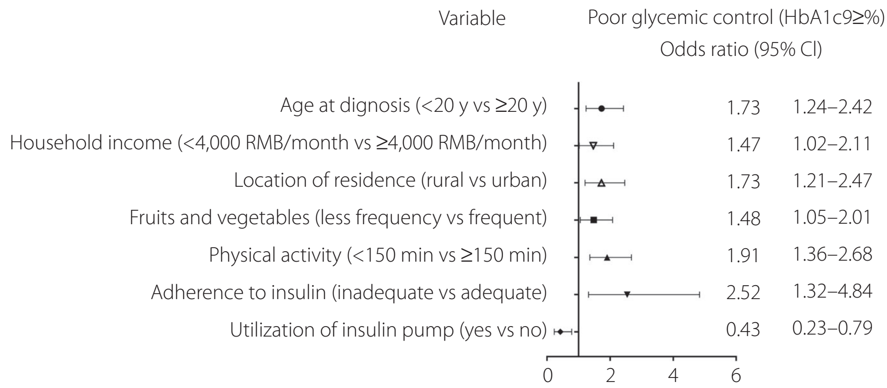

Figure 2 | Adjusted odd ratios and 95% confidence interval (CI) between risk factors and poor (hemoglobin A1c [HbA1c] ≥9%) glycemic control. Variables introduced in the multivariable analysis were age, sex, age at diagnosis, duration of diabetes, waist circumference, household income, location of residence, education level of family members, smoking status, diet control, intake of fruit and vegetables, physical activity, adherence to self-monitoring blood glucose, adherence to insulin, insulin regimen, and utilization of an insulin pump.

almost half of the participants did not consume the recommended amount of fruit and vegetables daily, which increased the risk of poor glycemic control. Similarly, in terms of physical activity, 40% of participants did not attain the recommended length of time. Low level of physical activity was independently associated with the increased risk of poor glycemic control in the present study, which is in line with other studies. A meta-analysis showed that physical activity could improve HbA1c, obesity, and lipid profiles among children and young people with type 1 diabetes[17]. This is mirrored in another study that included 18,028 adults with type 1 diabetes from Germany and Austria, which reported significant inverse associations between physical activity and HbA1c, BMI, diabetic ketoacidosis, dyslipidemia, and hypertension, as well as between physical activity and retinopathy or microalbuminuria[18].

The link between adherence and glycemic control has been investigated in several studies. Similar to other studies, the present results showed that low adherence to insulin was strongly associated with poor glycemic control. In 2013, Jill *et al.*[19], using data from the T1D Exchange clinic registry database, reported that excellent glycemic control was correlated with missing an insulin dose less frequently. An association between SMBG frequency and HbA1c was also observed in several other studies[20,21]. In the present study, we found that adherence to SMBG among people with type 1 diabetes under adequate glycemic control seemed to be better than those under poor control, but a statistically significant difference was not observed. The lack of a significant association between glycemic control and adherence to SMBG in the present study might be partly explained by the self-reporting method used to assess adherence. This method is more susceptible to recall bias and misreporting, which might overestimate adherence levels.

Insulin pumps represent the most intensive treatment of all regimens in type 1 diabetes. Pump use in type 1 diabetes has increased recently, which is driven by advancements in pump technology and awareness of the importance of controlling blood glucose to delay or prevent diabetes-related complications[2]. A meta-analysis including pediatric and adult studies found that pump use had a 0.6% (6.6 mmol/mol) greater reduction in HbA1c, as compared with multiple daily insulin injections therapy[22]. A large 7-year cohort study confirmed these findings by showing that pump therapy was associated with long-term lowering of HbA1c[23]. The present results are consistent with these showing that utilization of an insulin pump was related to a 58% lower risk of poor control. However, as compared with Western countries, the utilization rate of insulin pumps among type 1 diabetes population in China was relatively low[24], at just 11.4% in the present study. The rates of insulin pump use in different countries might reflect diversities in healthcare insurance, clinical practice and patient needs.

The strengths of the present study include the relatively large sample size covering all age groups that were recruited from multiple centers from two cities of China, and the examination of many demographic and clinical factors in relation to glycemic control. The present study, however, had some limitations. First, causality cannot be inferred in a cross-sectional study design and, ideally, the effect of factors on levels of glycemic control would be better explored using prospective longitudinal data. Second, single HbA1c values were used in our study, which only reflect glycemic control for the past 2 –3 months, and might have led to some individuals being inappropriately classified. Third, the population of China is heterogeneous, and our study population might not represent the rest of China. Fourth, not all participants had HbA1c tested at their visit. Our analysis was restricted to 91.8% of the study population whose HbA1c values were available. Fifth, HbA1c levels were tested at local hospital laboratories, which might influence the comparability of the results. Finally, islet cell autoantibodies were not tested in the present study, leading to possible misclassification of diabetes.

In conclusion, inadequate glycemic control is a common and widespread problem among people with type 1 diabetes in China. Efforts should be made to control the modifiable risk factors that include low intake of fruit and vegetable, low level of physical activity and low adherence to insulin for the improvement of glycemic control. Insulin pump use with adequate education of diabetes self-management among type 1 diabetes should also be encouraged. The findings of the present study emphasize the need to tailor interventions to people with early-onset type 1 diabetes and those who are socially disadvantaged.

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DISCLOSURE

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